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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/524,313

07/15/2005

David J. Rys

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02/26/2009

DANN, DORFMAN, HERRELL & SKILLMAN
1601 MARKET STREET
SUITE 2400
PHILADELPHIA, PA 19103-2307

EXAMINER

PURDY, KYLE A

ART UNIT

PAPER NUMBER

1611

MAIL DATE

DELIVERY MODE

02/26/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<i>Office Action Summary</i>	Application No.	Applicant(s)	
	10/524,313	RYS ET AL.	
	Examiner	Art Unit	
	Kyle Purdy	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 December 2008.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-33 is/are pending in the application.
- 4a) Of the above claim(s) 5-10 and 24-33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 11-21 and 23 is/are rejected.
- 7) ☒ Claim(s) 22 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2 pages (09/03/2008)</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application

1. The Examiner acknowledges receipt of the arguments filed on 12/18/2008.
2. Claims 1-4 and 11-23 are presented for examination on the merits. Claims 5-10 and 24-33 remain withdrawn. The following rejections are made.

Response to Amendment

3. The declaration under 37 CFR 1.132 filed 12/18/2008 is insufficient to overcome the rejection of claims 1-4, 11-21 and 23 based upon the rejection as set forth in the last Office action.

4. Applicants declaration is directed to illustrating that the instant meta-substituted compounds have improved solubility over the prior arts para-substituted compounds in a solvent matrix comprising 5% water, 85% ethanol and 10% propylene glycol. The Examiner acknowledges that the instant compounds possess the properties which Applicant is claiming. However, the declaration is insufficient to overcome the rejections of record. The declaration fails to illustrate why one would not attempt to formulate the instant compounds in a composition comprising water, ethanol and/or propylene glycol. Accordingly, the prior indicates that each of these three solvents, especially the latter two are commonly used in pharmaceutical formulations to solvate non-polar compounds for administration to a subject which are otherwise difficult to solubilize. It's taught that propylene glycol and ethanol are particularly useful solvents for solubilizing non-polar compounds that have minimal solubility in water. Knowing such, one of ordinary skill in the art would endeavor to formulate the instant compounds into a

composition comprising said solvents with a reasonable expectation for success in formulating the instant compositions.

Response to Applicants' Arguments

5. Applicants arguments filed 12/18/2008 regarding the objection to claim 22 made by the Examiner for an allowable claim as being dependent from a rejected base claim have been fully considered but they are not found persuasive. This objection is maintained. See response below.

6. Applicants arguments filed 12/18/2008 regarding the rejection of claims 1-4, 11-21 and 23 made by the Examiner under 35 USC 103(a) over Nitz et al. (WO 99/38508) in view of DeLuca et al. (Pharma. Dosage Forms Vol. 1; 1992) have been fully considered but they are not found persuasive.

7. The rejection of claims 1-4, 11-21 and 23 made by the examiner under 35 USC 103(a) is MAINTAINED for the reasons of record in the office action mailed on 07/02/2008.

8. In regards to the 103(a) rejection, Applicant asserts the following:

A) The solubility characteristics of the meta-substituted compounds claim in the application are superior to the corresponding para-substituted compounds, especially in solvent systems customarily used in electrohydrodynamic (EHD) delivery devices for pulmonary administration.

9. In response to assertion A, the Examiner acknowledges that the compounds have improved solubility in an EHD solvent matrix relative to the para-substituted compounds. Applicant is reminded that the composition comprising the EHD solvent system (85% ethanol, 10% propylene glycol and 5% water) as set forth in claim 22 has been indicated as allowable subject matter and is currently objected to. With respect to Applicants broader claim to a solvent matrix comprising ethanol, water and propylene glycol, this is still obvious in view of DeLuca. DeLuca

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is directed to parenteral formulations and carrier vehicles thereof. It's taught that when the compounds to be solvated are substantially non-polar, such as the instant compounds, waters presence in the composition is to be limited, especially if the compound is susceptible to hydrolysis. It's taught that co-solvents such as ethanol and propylene glycol are to be used to improve solubility of the non-polar compound. Thus, in view of DeLuca, one would have been motivated to formulate the instant compounds in a composition comprising water, ethanol and propylene glycol so that the compound was sufficiently solubilized for administration to a subject, wherein the composition had minimal amounts of water. Applicants arguments are not found persuasive.

Maintained Objections and Rejections, of record

Claim Objections

10. Claim 22 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Maintained Rejections

Claim Rejections - 35 USC § 103

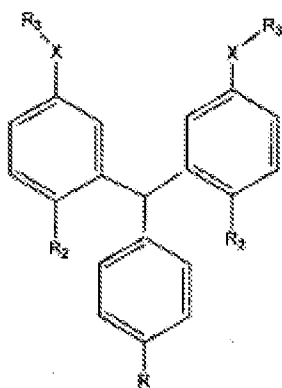
11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 1-4, 11-21 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nitz et al. (WO 99/38508; of record) in view of DeLuca et al. (Pharma. Dosage Forms Vol. 1: Parenteral Medications, 1992, 173-175; of record).

13. The claims of the instant application are drawn to a compound having the following structure wherein the species occupying the RI position is propyl. The compound is used in a pharmaceutical composition, in an amount effective to attenuate infectivity of pneumovirus. The composition further comprises at least one supplemental active agent such as interferons, immunoglobins, antibiotics, etc. The composition may comprise ethanol from at least 50% to at least 90% of the composition in addition to propylene glycol, and water. Preferably however, the composition comprises 85% ethanol, about 10% propylene glycol and less than 5% water.

14. The teaching of Nitz et al. ('508) is drawn to compounds, compositions and methods for treating or preventing pneumovirus infection and associated diseases. The compounds use to treat pneumovirus have the following structure



The species which may occupy the X, R, R₂ and R₃ are identical to those of the instant application in that X may be -C=N, R may be propyl, R₂ is hydroxyl, and R₃ is 5-methyl-1-tetrazolyl (see page 4, line 15 - page 5, line 5 and Example 10). The difference between '508

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and the instant application, R and R~ respectively, is the position of the substituent on the benzene ring. The substituent of '508 is in the para position whereas the instant applications substituent is in the meta position. Typically structural homologs, either isomers (i.e. cis vs. trans) or positional isomers (i.e. meta vs. para), often have similar pharmacological properties. With that stated chemists of ordinary skill would contemplate making slight variations of a known compound in order to obtain compounds with better and improved properties. The compounds of the prior art would motivate such routine organic synthesis and optimization, leading to the instantly claimed compounds which possess efficacy as inhibitors of pneumovirus replication. See *In re Deuel*, 51 F.3d 1552, 1558, 34 USPQ2d 1210, 1214. The teaching of '508 also stipulates for the inclusion of supplemental active agents such as interferons, antibiotics, and immunoglobins.

15. The reference teaches that the carrier solvent of the pharmaceutically active compound can consist of any "pharmaceutically acceptable carrier medium" meaning that the carrier includes any and all solvents. This would necessarily encompass and motivate the inclusion of ethanol, propylene glycol and water. Still, however, '508 specifically fails to include ethanol, propylene glycol, and water in the pharmaceutical preparation.

16. The teaching of DeLuca et al ('DeLuca) is drawn to parenteral formulations and useful carrier vehicles thereof. On page 175, Section B, it is noted that most parenteral products are aqueous solutions. However, inclusion of water may have to be limited if the active compound is susceptible to chemical degradation (i.e. hydrolysis, racemization, etc.). It is stated that for non-polar substances possessing limited solubility in water, it is necessary to use co-solvents such as ethanol and propylene glycol. Although DeLuca does not specifically teach adding the

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ingredients together in the amounts claimed. The amount of a specific ingredient in a composition is a result effective parameter that any person of ordinary skill in the art would desire to optimize. The instantly claimed percentages of said solvents, as described above, could readily be attained by routine experimentation and optimization.

17. Thus, it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to combine the teachings of '508 and DeLuca because in doing so one would create a pharmaceutically active formulation suitable for safe administration to a patient. The instantly claimed compound are obvious as they are structural isomers of reference '508 and one of ordinary skill in the art would be motivated to make such modifications with the expectation that the compounds and compositions thereof would possess identical pharmacological properties as those taught by the reference. Moreover, the use of water, ethanol, and/or propylene glycol as a carrier medium would be motivated by '508 statements that all pharmacologically acceptable carrier mediums can be used to carry the drugs. This motivates one to look to the prior art of drug formulations where is found that solvents such as water, ethanol and propylene glycol are commonly used as a carrier medium. Furthermore, the specifically claimed percentages of said carrier do not qualify as patentable subject matter, as these values could found via routine experimentation and optimization. Therefore, it would have been obvious to a person of ordinary skill in the art to combine the teachings of '508 with that of DeLuca with a reasonable expectation of success.

Conclusion

18. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

19. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kyle A. Purdy whose telephone number is 571-270-3504. The examiner can normally be reached from 9AM to 5PM.

21. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

22. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*/Kyle Purdy/
Examiner, Art Unit 1611*

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February 11, 2009

/David J Blanchard/

Primary Examiner, Art Unit 1643